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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,714	01/14/2000	YECHIEL SHAI	SHAI=2	4669

1444 7590 09/12/2003

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EXAMINER
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LUKTON, DAVID

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/12/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/367,714

Applicant(s)

SHAI ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-14, 20, 21, 27-35 and 37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 7-11 and 27-34 is/are rejected.
- 7) ☒ Claim(s) 2-6, 12-14, 20, 21, 35, 37 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

Pursuant to the directives of paper No. 26 (filed 7/3/03), claim 1 has been amended. Claims 1-14, 20, 21, 27-35, 37 remain pending. Applicants' arguments filed 7/3/03 have been considered and found persuasive in part. The rejection of claims 1 and 7 over Lakey (*Biochim Biophys Acta*, 1986) is withdrawn. Claims 1, 7-11, 27-34 are now rejected; claims 2-6, 12-14, 20, 21, 35, 37 are objected to because of their dependence on rejected claims.

✱

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 7-11, 27-33 are rejected under 35 U.S.C. §103 as being unpatentable over Shai (*J. Biol. Chem.* **271**, 7305, 1996).

As indicated previously, Shai teaches (p. 7308, col 1, 1st paragraph) that the peptide designated " (D)P<sup>7</sup>L<sup>18</sup>L<sup>19</sup> " is antibacterial but non-hemolytic. Shai does not disclose that if one of the amino acid side chains is extended by one methylene unit, that cytolytic activity will be retained, as directed to claims 1 and 7-11. However, a peptide biochemist of ordinary skill would have expected, *a priori*, that when a side chain of one amino acid in a peptide is extended by one methylene unit, the biological activity of that peptide will remain substantially the same [*In re Shetty* (195 USPQ 753) and *In re Hass & Susie* (60 USPQ 544)].

In the response filed 7/3/03, it is also argued that the claimed peptides must be non-hemolytic. However, this is not what the claims require. The claims do encompass peptides which are hemolytic, as long as the hemolysis occurs at a concentration which is "substantially higher" than that which is required to induce cytolysis of pathogenic cells.

In the response filed 7/3/03, it is asserted that Yechiel Shai is of the opinion that adding or deleting a single methylene unit from the side chain of an amino acid that is present in a peptide **may** abolish or reduce the biological activity of the peptide. However, no evidence to this effect has been made of record. In the event that such evidence is made of record, the relevance of this evidence to the claimed invention would then be assessed. An assertion that there may exist one or two peptides, unrelated to the claimed invention, which lose activity if a side chain is extended by one carbon atom would not be effective to overcome this ground of rejection.

Claims 27-33 are also rejected. Clearly, claim 27 is rendered obvious, since the reference discloses inhibition of bacterial growth; the microbiologist of ordinary skill would have been motivated to combine one of the disclosed peptides with a carrier in order to facilitate administration to a subject. The remaining claims (28-33) specify that the amount that is used must be effective to inhibit growth of fungi, or cancer cells, or viruses or protozoa. This ground of rejection is predicated on the assertion that the amount of peptide that is used by the microbiologist (to inhibit bacterial growth) will coincide with the amount necessary to inhibit growth of fungi, or cancer cells, or viruses or protozoa. The amount that is selected can occur over a wide range. The peptide could be administered to a mouse weighing 20 grams, or to a large mammal weighing several hundred pounds. Accordingly, a wide range of quantities of the peptide could potentially be useful to treat a bacterial infection. Thus, the artisan of ordinary skill would expect that somewhere along the spectrum of quantities, there would be an amount which is effective to inhibit growth of fungi, or cancer cells, or viruses or protozoa.

Thus, the claims are rendered obvious.

✱

Claim 34 is rejected under 35 U.S.C. §103 as being unpatentable over Shai (*J. Biol. Chem.* **271**, 7305, 1996).

Shai discloses (page 7306, table I) the peptides designated "(D)P<sup>7</sup>" and (D)L<sup>18</sup>L<sup>19</sup>. Also disclosed (page 7307) is that "(D)P<sup>7</sup>" is cytolytic (against *bacillus megaterium*) at a

concentration of 1.2  $\mu\text{M}$ , while at the same time is not hemolytic at this concentration. Similarly, Shai discloses (e.g., page 7307) that (D)L<sup>18</sup>L<sup>19</sup> is cytolytic (against *bacillus megaterium*) at a concentration of 0.6  $\mu\text{M}$ , while at the same time is not hemolytic at this concentration. Shai does not suggest combining two of the disclosed peptides for additive effects.

The microbiologist of ordinary skill recognizes that if a compound inhibits bacterial growth to a given degree at a given concentration, the compound will inhibit bacterial growth to an even greater degree at a higher concentration. This will be true up to a saturation point, above which additional compound will have no additional effect. But below the saturation level, the microbiologist of ordinary skill expects an "additive" effect for additional antibacterial molecules. This is true for a single compound, and is also true for two different compounds. If a "first" compound is antibacterial below its "saturation" point, then adding a "second" antibacterial compound will result in greater inhibition of bacterial growth than is the case for the "first" compound alone. Thus, the microbiologist of ordinary skill would have expected that by combining two of the antibacterial peptides of Shai, the result will be greater antibacterial effect (at a given concentration) than if just one peptide had been used.

Thus, the claim is rendered obvious.

✱

Claim 34 is rejected under 35 U.S.C. §103 as being unpatentable over Maloy (U.S.P.

5,792,831).

As indicated previously (Office action mailed 5/3/01) Maloy teaches cytolytic peptides containing D-amino acids. Also disclosed (e.g., col 5, line 30+) is that the peptides are not hemolytic. The reference does not teach combining two or more of the peptides for additive effects.

The limitations of claim 34 are met if there is motivation to combine two or more peptides that consist solely of D-amino acids, provided also that the peptides contain an "*alpha*-helix breaker moiety". As indicated on page 5, line 29+ of the specification, an *alpha*-helix breaker moiety would include simply the amino acid glycine. The disclosure of Malloy is replete with examples of peptides containing glycine. By way of example, most of the peptides listed at col 5, line 12+ contain a glycine, and moreover (col 5, line 30+) are not hemolytic.

The microbiologist of ordinary skill endeavoring to inhibit bacterial growth would have expected additive effects for two different antibacterial peptides, as explained above in the rejection of claim 34 over Shai (*J. Biol. Chem.*, 1996).

Thus, the claim is rendered obvious.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*D. Lukton* 9/10/03

*Christopher S. F. Low*

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